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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,011	02/17/2000	John Cooper Cox	017227/0155	6856
22428	7590	11/17/2003		EXAMINER
FOLEY AND LARDNER SUITE 500 3000 K STREET NW WASHINGTON, DC 20007				FOLEY, SHANON A
			ART UNIT	PAPER NUMBER
			1648	
			DATE MAILED: 11/17/2003	

35

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/506,011	COX ET AL.
	Examiner Shanon Foley	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 25 August 2003.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-3,6-8,12-17 and 53 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-3,6-8,12-17 and 53 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. §§ 119 and 120

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) All b) Some \* c) None of:  
1. Certified copies of the priority documents have been received.  
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) The translation of the foreign language provisional application has been received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                          | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>33</u> . | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

In paper no. 31, applicant amended claims 1-3, 6-8, 12-17, cancelled claims 4, 5, 9-11, and added new claim 53. Claims 1-3, 6-8, 12-17 and 53 are under consideration.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the limitation "adjuvant" in line 2. There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-3, 12-17 and 53 are rejected under 35 U.S.C. 102(a) as being anticipated by Berglindh et al. (WO 98/22135, provided with the IDS submitted 8/25/3), as evidenced by Cox et al. (Vaccine. 1997; 15 (3): 428-256).

The claims are drawn to an immunogenic complex comprising a negatively-charged organic complex, which comprises a saponin and a sterol, and a charged antigen. The organic complex and the antigen are electrostatically associated. The organic complex comprises a phosphoglyceride, such as phosphatidyl inositol or phospholipid A. The immunogenic complex induces a CTL response when administered.

Berglindh et al. anticipate a pharmaceutical formulation comprising a negatively charged lipid complex and an antigenic peptide that are electrostatically associated. The lipid is a phospholipid, such as phosphatidyl inositol, see claims 1 and 9-11 and page 11 lines 8-13.

Cox et al. review adjuvants on pages 251-253 and teach that complexes comprising saponin and sterols inherently induce a Th1 and Th2 responses against antigens incorporated into them. Therefore, although Berglindh et al. do not teach an induction of a CTL response, the composition of Berglindh et al. comprise all of the material ingredients required to induce such a response, as evidenced by Cox et al.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 53 is rejected under 35 U.S.C. 102(e) as being clearly anticipated by Popescu et al. (US 5,897,873). This claim is also rejected under 35 U.S.C. 102(e) as being clearly anticipated by Popescu et al. (WO 90/

The claim is drawn to an immunogenic complex comprising a negatively-charged organic complex and a charged antigen that are electrostatically and induce a CTL response.

Popescu et al. clearly anticipate an immune complex comprising lipid A comprising phosphatidic acid or phosphatidyl glycerol that is electrostatically associated with a positively-charged antigen, see column 3, line 65 to column 5, line 5 and lines 35-37, column 8, lines 11-15 and claims 1-8. This complex of Popescu et al. also induces a CTL response, see column 2, lines 5-16.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berglindh et al. light of Cox et al., as applied to claims 1-3, 12-17 and 53 above, and further in view of Callahan et al. (Pharmaceutical Research. 1991; 8 (7): 851-858).

The claims state that the organic complex and the antigen have been modified to increase their respective charges.

See the teachings of Berglindh et al. The reference does not teach modifying the organic or the antigen to increase their charges.

Callahan et al. teach the importance of surface charge in antigen-adjuvant complexes and clearly demonstrates that there is enhanced adsorption between a positively charged antigen and a negatively charged adjuvant, see the entire reference.

One of ordinary skill in the art at the time the invention was made would have been motivated to incorporate positively charged antigens and negatively-charged adjuvants to increase antigen adsorption into the adjuvant carrier matrix. One of ordinary skill in the art at the time the invention was made would have also been motivated to augment the complementary isoelectric charges of each antigen/adjuvant component to increase antigen incorporation into the adjuvant. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for increasing adsorption of positively-charged antigens into negatively-charged adjuvants Callahan et al. and Cox et al. teach that the respective adjuvants incorporate antigens into the matrix. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Applicant argues that there is no suggestion in Callahan et al. to modify the charge association of an organic complex and an antigen. Applicant asserts that the prior art modifies protein hydrophobicity to be incorporated into ISCOMs. Applicant asserts that the skilled artisan would not have been motivated to pursue electrostatic associations.

Applicant's arguments have been fully considered, but are found unpersuasive because Callahan et al. emphasizes the importance of the strength of electrostatic association and adsorption of the antigen within a negatively charged adjuvant. This principle of increased adsorption applies to any antigen when it is electrostatically associated with any negatively-charged adjuvant, regardless of whether the adjuvant is organic or inorganic. Therefore, it is maintained that the ordinary artisan would have been motivated to increase the respective charges of the adjuvant and the antigen to increase antigen adsorption into the adjuvant.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 6-8, 12-17 and 53 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of copending Application No. 09/714438 for reasons of record.

Applicant states that this rejection will be officially addressed upon notification of allowable subject matter. Applicant's statement is noted and until such time, this rejection is maintained.

***Conclusion***

Applicant's amendment and the IDS, submitted 8/25/03 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

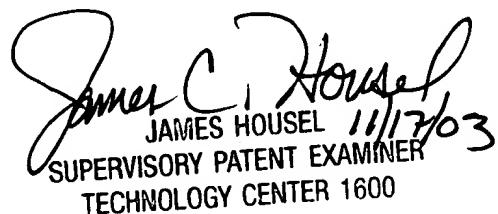
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Shanon Foley



JAMES HOUSEL 11/17/03  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600